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Diagnosis of leprosy in skeletons from an English later Medieval hospital using histological analysis

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Abstract

The diagnosis of leprosy in skeletal materials from archaeological sites can be problematic. Periostitis on the tibiae and fibulae is commonly seen in leprosy, in addition to other expected changes (e.g. alterations around the anterior bony aperture of the nose). However, periosteal new bone formation could be caused by a number of conditions. This paper describes the histological analysis of thin ground sections of tibiae with periosteal new bone formation from six individuals diagnosed with leprosy from a later Medieval hospital site in Chichester, England. In addition, one individual from a later medieval priory site on Lihou Island, Guernsey, with no characteristic lepromatous leprosy bone changes was examined. The aim was to determine, by light microscopic analysis of thin ground sections, whether the changes on the tibiae had been the result of leprosy or another condition. Results showed that there is a high probability that a specific histological appearance is characteristic of leprosy; for differential diagnoses, endemic syphilis is discussed.

Keywords

Leprosy, tibial periostitis, differential diagnosis, histology

1. Introduction

According to documentary sources, leprosy was a relatively common occurrence in later Medieval Europe (Richards, 1977). However, as with so many apparently frequent diseases, the number of cases diagnosed in archaeologically derived skeletal material from all areas of Europe, but particularly England, is low (see Roberts, this volume). There may be many reasons for this. Firstly, if people contract the high resistant (tuberculoid) form of the infection they may not develop any bone changes. Secondly, people with leprosy may have died before there was time for bone change to occur. In both these scenarios, the evidence would be absent skeletally (see Wood *et al.*, 1992 for discussion). Thirdly if, as suggested in contemporary sources, people with leprosy were isolated from the rest of the community into leprosy hospitals, then we may only expect to see cases in the cemeteries associated with those institutions. Few leprosy hospital cemeteries have been excavated in England (Roberts, 1994) although, paradoxically, lepromatous individuals

have been identified in non-leprosy hospitals (Roberts, this volume). Fourthly, leprosy may not have been as common as suggested, and this may be related to misdiagnosis, i.e. people with another disease may have been labelled as leprosy. Finally, the diagnosis of leprosy in skeletal material can often be hampered by poor preservation and excavation of facial, hand and foot bones, and lack of experience on the part of the observer. In addition, there may be several diagnoses that could be applied to the individual bone changes observed in leprosy.

When diagnosing leprosy, most researchers follow the guidance of Møller-Christensen (1961), Andersen and Manchester (1987, 1988, 1992), and Andersen *et al.* (1992, 1994). The focus is on the primary (or pathognomonic) changes of *facies leprosa* (Møller-Christensen, 1974) or the rhinomaxillary syndrome (Andersen and Manchester, 1992), seen in lepromatous or near lepromatous individuals. This consists of anterior nasal spine absorption, nasal aperture remodelling, inflammation of the palate, recession of the alveolar process of the maxilla, loss of the anterior teeth and sometimes lack of

development of anterior maxillary tooth roots (leprogenic odontodysplasia – Danielsen, 1970). Secondly, the hands, feet and lower legs may be affected as a result of bacterial invasion of the sensory, motor and autonomic nervous systems. This can result in: absorption of the distal ends of the terminal hand and foot phalanges, metacarpals and metatarsals, knife-edged remodelling of the metatarsals, concentric atrophy of the metacarpals, metatarsals and phalanges, “nicking” of the distal ends of the distal hand phalanges, periostitis, osteitis and osteomyelitis of hand and foot bones, septic arthritis of the foot and hand joints which may lead to fusion, cup and pencil deformities of the metacarpo-phalangeal and metatarso-phalangeal joints, associated with osteoporosis of the hand and foot bones, flexion deformities (indicated by “grooves”) in the hand and foot phalanges, and dorsal tarsal bars of bone (indicating collapse of the arches of the feet and consequent strain on the ligaments). Additionally, the lower legs may develop a periosteal reaction in the form of new bone formation on the tibial and fibular shafts (Lewis *et al.*, 1995).

Because the skeleton can only react in a limited number of ways to disease, many disease processes (bone formation, bone destruction, or both) can produce similar changes in the skeleton, and patterning of the changes is key in attempting a diagnosis. There are a number of differential diagnoses that need to be considered for the changes thus described. Tuberculosis and the treponemal diseases of yaws and venereal syphilis may affect the rhinomaxillary area (Manchester, 1994). The changes in the hands and feet may also be caused by the joint diseases such as psoriatic and non-specific septic arthritis (Rogers and Waldron, 1995), and conditions that lead to flexion deformities of the hands and feet such as congenital claw-hand, and dorsal tarsal bars caused by flatfootedness (*pes planus*), pyogenic osteomyelitis, frostbite and diabetes mellitus (Aufderheide and Rodríguez Martín, 1998). The lower leg periostitis may also be the result of a number of conditions such as non-specific infection, which may be the result of “stress” (Goodman *et al.*, 1988), trauma (Ortner and Putschar, 1981:132), treponemal disease (yaws, endemic and venereal syphilis) – Steinbock (1976), primary and secondary hypertrophic osteoarthropathy (Resnick, 1995:4425), vitamin C deficiency (Aufderheide and Rodríguez Martín, 1998:311), overlying soft tissue infection (Ortner and Putschar, 1981:131), including venous stasis (Resnick, 1995:4425), and infantile cortical hyperostosis (*ibid.*). These problems of differential diagnosis emphasise the need to consider the distribution pattern of abnormal lesions in the skeleton, in addition to considering them together, rather than in isolation.

It is understood that the lower leg changes are usually a result of the transmission of secondary infection due to leprosy from the feet up to the lower legs. However, if the lower legs are affected, but not the rest of the skeleton, then a specific diagnosis is more difficult. This paper describes an attempt to diagnose leprosy purely based on the histological changes in sections of tibiae from five

known leprosy cases, plus one individual with no evidence of a specific infection.

2. Material and Methods

Six skeletons were selected from the cemetery associated with the later Medieval hospital at Chichester, England, a hospital that was initially opened for leprosy sufferers in the 12th century AD (Lee and Magilton, 1989). All the skeletons showed diagnostic changes of leprosy, but also included tibial new bone formation. Based on accepted criteria (Buikstra and Ubelaker, 1994), five males and one probable female were identified, and all were adults ranging from young to older age; these data are summarised in Table 1.

All the skeletons were well preserved, although two (64, 202) were fragmentary. Diagnosis of leprosy was based on macroscopic criteria as outlined above and Table 2 summarises the features used.

In addition to the bone changes of leprosy, other pathological changes were noted, although they are not directly relevant to this study. The young adult male from burial 21 displayed cribra orbitalia, dental disease, Schmorl's nodes in the spine, and Harris' lines in the tibia. The mature adult male from burial 48 shows a number of dental diseases, Schmorl's nodes and spinal joint disease, and healed fractures of three ribs. The adolescent to young adult male from burial 64 presents dental disease and Schmorl's nodes. The young to middle adult male from burial 88 had evidence of dental disease and Schmorl's nodes in addition to maxillary sinusitis, non-specific infection of the radii, ulnae and metacarpals (possibly associated with leprosy – see Lewis *et al.*, 1995), while the young- to middle adult male from burial 148 similarly showed dental disease and Schmorl's nodes plus periostitis of the visceral surface of the ribs, and osteoarthritis in the hands and feet. Finally, the young- to middle adult probable female from burial 202 had evidence of dental disease, Schmorl's nodes, and osteoarthritis in the hip and rib joints.

Further to the six skeletons described above, another skeleton from a later medieval priory site on the Island of Lihou, Guernsey, was included in the analysis. This well preserved skeleton was from a male aged between 26 and 45 years at death who suffered from osteoarthritis of the spine, right clavicle and scapula, dental disease (enamel defects, calculus, caries and a maxillary torus), and some fused foot phalanges. Additionally, he had florid longstanding new bone formation on the tibiae and fibulae. The reason for including this individual in the analysis was because of the lack of any changes in the skeleton that would indicate a specific disease, including leprosy. With respect to leprosy, there were no changes to the facial, hand or foot bones, but lower leg periostitis was evident. The tibiae that showed periosteal new bone formation on their surfaces were selected. The tibial shafts were cross sectioned and 6 to 10 mm thick slices were taken for

histological analysis. Thin ground sections of 50µm or 70µm were used. It is considered that morphological structures are only visible and detectable in polarised light when the section is 50µm or thicker. Of course, this is not the normal thickness used in histopathology when cells and other tissues still survive, and the section thickness is usually much reduced. Furthermore, decalcification of bone, as seen in modern histopathology, is not appropriate for archaeological bone for various reasons (e.g. see Schultz, 1986, 1997).

Only in the male from Lihou was a small sample (size 8 x 5 mm) taken for scanning-electron microscopy before embedding the rest of the bone section for light microscopy. For the individuals 64, 88, 148, and 202 from Chichester the right tibia was selected, and for individuals 21 and 48 from Chichester and the male from Lihou the left tibia was selected for sectioning. Figures 1-5 show the macroscopic and radiographic changes of the Chichester samples. Following sectioning of the bones, the samples were subjected to the embedding process and thin ground sections were produced by the techniques described by Schultz and Drommer (1983) and Schultz (1988). Histomorphological age was established by the methods of Kerley and Ubelaker (1978) and Wolf (1999), but also by accepted morphological methods described by Buikstra and Ubelaker (1994).

3. Results

3.1 Chichester burial 21

A complete cross section was taken from the middle of the left tibia shaft. From the proximal (Plate 1/A and Figure 7) and distal end of this section (Plate 1/B and Figure 6) thin ground sections were produced. More specifically, particularly on the external area of the shaft (external circumferential lamellae) of this well preserved tibia, bone collagen is present. In the other parts of the cross-section, almost no collagen has been preserved. Thus, the preservation is relatively good in parts of the bone. The histomorphological age determination suggests an individual age of approximately 20-25 years.

The external surface of the lateral aspect of the shaft, anterior to the interosseous margin, protrudes only slightly, whereas the surface of the medial aspect protrudes severely. The structure responsible for the "protrusion" consists of a relatively thin lamellar structure (maximum thickness is 1mm) which does not represent the original bone surface (= external circumferential lamellae), but rather a secondary layer of bone of periosteal origin caused by a pathological process. The layer which shows a very well organised stage of remodelling (Figure 6), covers the primary external circumferential lamellae and the original compact bone substance like the bark of a tree. Thus, there is a very fine borderline between the newly built bone and the original circumferential lamellae (Figure 7). This line does not represent the *grenzlinie* found in shafts of long bones affected by treponemal disease (cf. Schultz and

Teschler-Nicola, 1987, Schultz, 1994). There are also no structures suspicious of polsters which are a criterion of treponemal diseases (cf. Schultz and Teschler-Nicola, 1987, Schultz, 1994). The morphology of the periosteal newly built bone indicates a slowly developing chronic inflammatory process from which the person probably suffered for several years. In the distal area of the shaft, the newly built bone was thicker (Figure 8). However, due to diagenesis, the layer is severely eroded. Nevertheless, the microscopic analysis reveals that this part of the new bone is of woven type which means that this layer is more recent than the one described before (Figure 6). Thus, the periosteal changes apparently represent a recurrent process.

3.2 Chichester burial 48

This bone sample represents a complete-cross section through the distal metaphysis of the left tibia. Macroscopically, the bone seems to be well preserved. However, at the microscopic level, the preservation is fair to poor. Only a few areas of bone collagen are visible. The age calculated by histomorphology is 60 years or more.

However, the osteoporotic change in the compact bone substance and of the cortical bone (maximum thickness is 2mm), as well as the extreme rarefaction of the spongy bone trabeculae, could also be caused by atrophy due to inactivity and not only ageing (Plate 1/C, Figure 9). Almost all of the circumferential bone surface is covered by a secondary layer of bone which represents periosteal new bone formation (Plate 1/C). These structures are secondarily well remodelled and changed by the osteoporotic process (Figure 10). Middle and high magnification microscopy (25x, 100x) reveals that the periosteal bone formation on the antero-lateral surfaces, and probably also on the dorsal face of the bone, was built up in at least two layers (Figure 10). This means that the pathological process, which was probably of inflammatory origin, was characterized by signs of recidivation.

3.3 Chichester burial 64

A small sample from the right tibia representing, in the cross section, only one fourth of the circumferential part of the shaft, probably from the medial face, was analysed microscopically (Plate 1/D). The preservation is poor, and no bone collagen was preserved. A histomorphological age determination was not possible because of the small size of the sample and poor preservation. The compact bone covering the spongy bone was very thin (maximum thickness is 3mm, minimum thickness is 1mm). This sample was probably taken from the metaphysis of the bone.

The external bone surface slightly "bulges". The changes are reminiscent of polster-like structures (Figure 11). Thus, there is only evidence of a very slight periosteal reaction as a result of an inflammatory process which is very well organised, i.e. remodelled. The thin newly built bone formation seems to have grown out of the original compact

bone substance which was not affected in any way.

3.4 Chichester burial 88

A complete cross-section was taken from the middle of the shaft of the right tibia of this individual; it was relatively brittle and had been broken in several places. Microscopic analysis revealed extremely little evidence of bone collagen. Because of the poor preservation, histomorphological age determination gave only an approximate idea of the age of the individual which can be calculated as probably older than 30 or 35 years.

Low and middle magnification microscopy (10x, 25x) illustrate that the compact bone substance of the antero-medial face of the shaft is affected by osteoporosis which is very probably not due to the age, but caused by a pathological process of the medullary cavity (Plate 1/E). The rest of the cross-section of this tibia seems to be affected only very slightly by this process. The medullary cavity is enlarged which could be due to ageing, but also to the pathological process.

High magnification microscopy (100x) shows that the osteoporotic area was apparently caused by an inflammatory process, which affected not only the compact bone substance (osteitis), but also the medullary cavity (osteomyelitis) and the periosteum (periostitis). This periosteal new bone formation is mainly expressed on the external surface of the anterior half of the tibia, particularly on the medial aspect of the shaft (Plate 1/E), medially and laterally to the anterior margin. The changes, which are the product of a florid inflammatory process of the periosteum, are composed of woven bone and no bone remodelling is evident (Plate 1/E, Fig. 12). In the dorsal half, and also in the antero-lateral area of the shaft, the external surface of the tibia "bulges". In this region, the compact bone substance of the tibia is relatively thick (6mm). However, the external half of the compact bone substance (thickness is approximately 3mm) represents a remodelled area which was primarily an external, i.e. subperiosteal bony layer caused by a pathological process. Whether this last change described was the result of an inflammatory or a hemorrhagic process cannot be determined. This is because of remodelling of the original bone layer, which is now completely integrated into the compact bone substance, and the postmortem lack of the bone collagen. However, in middle and high magnification microscopy (25x, 100x), this remodelled layer on the external bone surface in the antero-lateral face of the shaft shows structures which resemble the polsters (Figure 13), characteristic in chronic treponemal disease (Schultz and Teschler-Nicola, 1987, Schultz, 1994). There is no visible demarcation between the periosteal new bone formation and the original compact bone, probably because of the poor preservation of the bone collagen. However, at the base of the new bone formation, some small and narrow blood vessel canals, which are orientated in a line parallel to the external bone

surface, suggest a possible demarcation.

There are at least two suggestions for classifying the two different periosteal changes:

- 1) an acute (active) phase of an inflammatory process of the periosteum (periostitis) demonstrating rapid growth, which was apparently induced by an osteomyelitic-osteitic process
- 2) a chronic and mainly slowly changing process of probable inflammatory origin in the stage of remodelling which does not represent a typical florid haematogenous osteomyelitis
- 3) Theoretically, there is also a third possibility. Both processes could be due to the same disease. In this case, the second, relatively fresh periosteal reaction only represents the product of a recidivation. However, the different nature of these changes renders this not very probable.

3.5 Chichester burial 148

A complete cross-section from the middle of the shaft of the right tibia was taken for microscopic analysis. Macroscopically, the bone is well preserved whereas, on the microscopic level, preservation is poor because of the lack of bone collagen. Only in some "patch-like" structures in the middle of the compact bone substance, are there remains of bone collagen. The histomorphological age determination yields a result of between 40 and 55 years.

The external surface of the shaft "bulges" on its medial and lateral face (Plate 1/F). These areas are characterized by secondary new bone formation, which has an average thickness of 1.5mm and is well organised. On the lateral face, between the interosseous and anterior margins, this bone has a maximum thickness of 2.5mm, while all the compact bone, including the newly formed bone, measures only 4.6mm. The original periosteal layer presents in some areas small polster-like structures and is partly very well integrated into the original compact bone substance (Figure 14). In some other areas, however, there are remains of a very fine demarcation line between the original external bone surface and the periosteal new bone. This line is not comparable with the *grenzlinie* which is frequently found in chronic treponemal disease (cf. Schultz and Teschler-Nicola, 1987, Schultz, 1994). It seems that this inflammatory process was present for many years.

The original compact bone substance and the medullary cavity has not been affected by a pathological process. However, in the middle of the compact bone substance there are "field-like" areas of tangential lamellae which probably represent the result of inactivity atrophy (Figure 15).

3.6 Chichester burial 202

Macroscopically, the complete cross-section from the middle of the shaft of the right tibia, which is a relatively gracile bone, is fairly well preserved and shows no distinct vestiges of periosteal reaction (Plate 1/G). Microscopically, the bone is fairly well preserved. However, only very few remnants of bone collagen are observable. The histomorphological age determination suggests an individual of between 35 and 45 years.

On the medial aspect of this bone, there is a superficial small striated zone on the periphery of the original compact bone substance resembling a secondary layer. This structure is difficult to explain by analysis at low magnification analysis (10x). In this area, the original compact bone substance measures 3-3.5mm in thickness, whereas the external striation has a thickness of only approximately 1mm. However, middle and high magnification analysis (25x, 100x) reveals that this superficial layer, which has a bark-like character, is very well organised as lamellar bone and represents the vestiges of an extensive, remodelled periosteal reaction. Thus, the new bone formation was probably built up layer by layer over a relatively long time. A very similar structure is seen on the lateral aspect of the tibial shaft, anterior to the interosseous margin. Here, the border between the original external bone surface and the new bone formation, which is very well integrated into the compact bone substance, is still visible by the orientation of small, narrow and tangentially orientated blood vessel canals (Figure 16).

3.7 The male from Lihou

In the cross section, the left tibia is relatively normal in size. Microscopic analysis suggests that the preservation is poor to fair. There are relatively slight and diffuse vestiges of diagenesis (Plate 1/H). The destruction was apparently caused by algae and/or fungi (cf. Schultz 1986, 1997). The bone collagen is more or less totally destroyed by these postmortem changes; this makes diagnosis difficult. However, in some small areas of the original compact bone, remains of collagen are still seen. A reliable histomorphological age determination cannot be made, but a trend can be noted. In the original compact bone, the size of the Haversian canals and of the Haversian systems, and the distribution of the latter indicate an individual age of approximately 25 to 39 years. The medullary cavity is relatively large (Plate 1/H). On the dorsal face of the shaft, the compact bone measures 5.7mm in thickness, and on the lateral face only 3mm, excluding the new bone formed (Plate 1/H). There are also relatively broad tangential lamellae (Figure 17) and relatively wide resorption lacunae, which should not be diagnosed as due to ageing, but as characteristic features of inactivity atrophy, probably due to disuse of the leg because of the pathological process.

At low and middle magnification microscopy (10x, 25x), the bone demonstrates an obvious pathological feature.

There is an irregularly structured, secondary bony layer of porotic character (Plate 1/H), which is responsible for the bulging of the external face of the shaft (Figures 18 and 19). On the medial face of the tibia, the layer is relatively thick (maximum thickness is 2.3mm) and represents a moderate stage of a periosteal reaction which was not very longstanding when the person died. This means that the layer was in an earlier stage of remodelling, whereas the newly formed bone on the lateral aspect of the shaft is only very thin and represents an old, very well organised, advanced stage of remodelling. Thus, the changes on the lateral aspect of the bone started at least several years before the death of this man. These newly built formations seem to be partly deposited on the original bone surface, and partly growing out of the compact bone substance around the periphery of tibia shaft (Figure 20). The remodelled layer shows structures which resemble the polsters (Figure 19) characteristic of chronic treponemal disease (Schultz and Teschler-Nicola, 1987, Schultz, 1994). Furthermore, and only visible by microscopic analysis, the original layer is partly demarcated against the original compact bone substance by a line of small and narrow blood vessel canals. A typical *grenzlinie* is not present, but in small areas of the section lamellar bone resembles this structure, characteristic of chronic treponemal disease. The character of the new bone formation suggests a slowly growing process, because there are no features of rapid bone growth such as small bone spicules (Plate 1/H). A recidivation of an inflammatory process is very probable.

The original compact bone substance apparently shows no convincing evidence of *intra vitam* changes such as bone remodelling (Plate 1/H). However, a slight affection of the compact bone cannot be completely excluded because, almost throughout the compact bone substance, there are two narrow cord-like structures which are rectangularly orientated to the external bone surface (Figure 21). These structures resemble changes seen in cicatrised metaplasia. There is no evidence of involvement of the medullary cavity such as is seen in inflammatory processes. Thus, a typical periostitis such as a florid inflammatory process, does not seem to be very probable.

4. Discussion

Although the sample of skeletons used for this study was small, and the features described are not pathognomonic to leprosy, this is the first attempt to describe histological changes of bone alteration associated with leprosy. The tibiae of the six individuals from Chichester, and of the male from Lihou, show characteristic signs of periosteal bone reaction which are macroscopically and microscopically very similar, or even identical, in all examined cases. Thus, there is a high probability that the changes were caused by similar, or the same, processes. However, this does not necessarily mean that the people suffered from the same diseases, because sometimes different diseases can produce similar or almost the same morphological changes in the bones (especially as bone

can only react in a limited number of ways to inflammation). This is one of the main problems in paleopathology. As a rule, paleopathologists can only examine signs of ancient disease in macerated, i.e. dry bones. Thus, no soft tissues or cells, which play an important role in pathological investigations in the living, can be studied to establish a reliable diagnosis or for comparative purposes. This means that diagnostic criteria are sometimes relatively limited in paleopathology. On the other hand, reliable diagnoses can be established by using different characteristic signs which are not easy, or are even impossible to study in living patients or in recent-pathological specimens. At the microscopic level, there are such characteristics, such as faserfilz-osteon (e.g. in a primary bone tumour), polsters and/or grenzlinie (in treponemal disease).

Up to now, very little histopathological analysis of ancient leprosy bones has been undertaken. It is not possible to diagnose leprosy by using only a bone section taken from the shaft of a tibia. However, it is possible to compare periosteal reactions at the microscopic level with the well-known characteristics of hematogenous osteomyelitis, treponemal disease, tuberculosis and even non-specific periosteal reactions such as inflammatory processes of the deep veins, primary and secondary hypertrophic osteoarthropathy (i.e. Bamberger-Marie disease, which could be caused by chronic heart-lung diseases) and scurvy in ancient skeletal material. Additionally, overlying soft tissue infections can produce a periosteal lesion. As a rule, it is not too difficult to differentiate between the bony products of an inflammatory or a hemorrhagic process (Schultz and Teschler-Nicola, 1987, Schultz, 1993). However, frequently both processes are mixed and this makes diagnoses again difficult (Schultz, 1993).

In recent literature describing the morphological changes in leprosy, emphasis is placed on the structural changes of the soft tissues (e.g. Waters, 1990), whereas macroscopic changes on bone surfaces and characteristic features of the micro-structure of dry bone specimens are neglected. Therefore, paleopathologists who intend to examine leprosy skeletons are advised to study the reports on pathological investigations at the macroscopic (Hirschberg, 1923, Klingmüller, 1930), microscopic (e.g. Sawtschenko, 1891, Beitzke, 1934) and radiological (e.g. De La Camp, 1900, Deycke Pascha, 1906) levels carried out at the end of the 19th century, and into the first half of the 20th century. These papers are extremely helpful because of the sophisticated and detailed description of morphological features in leprosy bones.

All thin ground sections produced from the seven samples were checked for characteristic features. Nature, frequencies and distribution of the microscopic bone changes and the characteristic features in the cross sections of these tibiae demonstrate an extensive similarity (Table 3). It is also important to bear in mind that all individuals from Chichester macroscopically showed the well-known features of leprosy in the skull. They also had changes

characteristic of this disease in the postcranial skeleton, that is in the hands and/or the feet (Table 2). The probable female only has changes in the skull. The male from Lihou shows neither leprosy changes in the skull nor in the hands and feet (Table 2).

All individuals examined in this study suffered from a periosteal reaction of the tibia. In all of these cases, the periosteal reaction was longstanding which had been well remodelled probably years before the death of the individuals (Figures 6, 9, 11, 13 and 16). In six of the seven cases, the new bone formation apparently grew relatively slowly. Only in one case (Chichester burial 48) can the nature of the growth not be estimated (Figures 9 and 10). Additionally, in two of the seven individuals, new bone formation could also be observed (Chichester burial 88 and the Lihou male). In the male from Lihou, some parts of the new bone formation were already in the early stage of lamellar organisation (Figure 19), whereas in the individual from Chichester (burial 88) the new bone consisted of woven bone (Figure 12). The changes in the latter case represent relatively rapid bone formation. Thus, in both cases, the nature and the type of bone formation was apparently different (cf. Plate 1/E and H). The new periosteal bone formation on the distal end of the tibia of the Chichester individual from burial 21 (Figure 8) represents a level of development which is comparable to that of the Lihou male (Figure 20). However, as described before, in the Lihou male the stage of development was not the same in all parts of the bone formed (compare Figure 19 with Figure 20). Furthermore, in three cases (Chichester burial 48 and probably also burial 21, as well as the male from Lihou) the periosteal bone formation showed vestiges of recidivation (Figure 10).

Only in one individual (Chichester burial 88), was the medullary cavity affected by the inflammatory process (Plate 1/E). In one of the individuals from Chichester (burial 48), the cause of the enlargement of the medullary cavity was osteoporosis due to age (Plate 1/C). In the male from Lihou, there was a slight enlargement of the medullary cavity which cannot be really interpreted (Plate 1/H). A possible cause could be disuse atrophy. In the individual from Chichester burial 88, the compact bone was affected in the same way as the medullary cavity. There are signs of an inflammatory process in the form of osteolysis, producing osteoporosis of the compact bone (Plate 1/E). In the individual from Chichester burial 48, the reduction of the compact bone of the tibial shaft was due to osteoporosis related to age (Plate 1/C). Slight changes in resorption, mainly in the endosteal area of the compact bone substance, are again probably due to disuse atrophy.

Special features indicating different stress markers, or even diseases, were observed at the microscopic level in the cross-sections of the seven individuals. The tangential lamellae which were found in the middle of the compact bone substance of the tibia of the individual from Chichester burial 148 (Figure 15), and of the Lihou male (Figure 17) are indicators of chronic inactivity atrophy

(Schultz, 1986, cf. Knese *et al.*, 1954). These structures need years for their development. In the Lihou male, these structures correlate with the reduction of the compact bone substance and the enlargement of the medullary cavity. In the individual from burial 48, tangential lamellae could not be found because of the extreme rarefaction of the compact bone substance due to old age involution.

Polsters are characteristic features at the microscopic level which are frequently found in chronic treponemal disease involving the long bones (Weber, 1927, Michaelis, 1930, Schultz and Teschler-Nicola, 1987, Schultz, 1994). In particular, well developed polsters are a good indicator of treponemal disease (Schultz, 1994). However, in three of the six cases from Chichester (burials 64, 88 and 148) which show the bony lesions of leprosy, and also in the skeleton of the male from Lihou, there are no typical polsters but only polster-like structures which are rudimentarily developed and relatively flat. At the microscopic level, polster-like structures were also detected by Blondiaux (pers. comm., cf. Blondiaux *et al.*, 1994, Blondiaux *et al.*, this volume) in medieval skeletons showing the bony signs of leprosy.

As a rule, a grenzlinie can also be observed in chronic treponemal disease which is not found in hematogenous osteomyelitis of long bones (Schultz and Teschler-Nicola, 1987, Schultz, 1994). Thus, a grenzlinie could also be a useful indicator for diagnosing chronic treponematosis using microscopy. In this investigation, faint signs of a possible grenzlinie were observed in at least two, or even three, of the six cases from Chichester (burials 21, 148 and possibly 88) as well as in the skeleton of the male from Lihou. However, the features were very subtle and only visible with difficulty. In contrast to these findings, in treponemal diseases including endemic syphilis, there are not only alterations in the subperiosteal bone, but additionally also osteoclastic changes in the endosteal bone and the bony trabeculae of the medullary cavity, as well as in the compact bone substance of the shaft of the affected long bones (Schultz and Teschler-Nicola, 1987, Schultz, 1994, Kuhnen *et al.*, 1999).

When we come to the differential diagnoses and the basic etiology of these lesions there are principally two possibilities:

1) We have to bear in mind that all six individuals from the Chichester cemetery suffered from chronic bone changes of leprosy, seen in the well-known macroscopic lesions of the face, and in the hands and/or feet. Additionally, all these individuals showed signs of a periosteal reaction on their tibiae which could be primarily characteristic of leprosy (cf. Møller-Christensen, 1974, Steinbock, 1976, Ortner and Putschar, 1981, Resnick, 1995, Aufderheide and Rodríguez Martín, 1998). The skeleton of the male from Lihou showed no signs of leprosy, but also presented periosteal new bone formation. This makes a diagnosis of leprosy also possible.

2) On the other hand, it could be argued from the morphological features resembling polsters and grenzlinie, that the periosteal reaction was caused by treponemal disease, probably endemic syphilis (cf. Schultz, 1994, Kuhnen *et al.*, 1999). Thus, all seven individuals could have been affected by this treponematosis, suffering additionally from leprosy which was proved by the bony changes in the face, the hands and/or the feet.

Indeed, with respect to the first possibility, at the microscopic level, the periosteal new bone formation in the tibiae are different from that observed in treponemal disease. Thus, these changes may primarily not be caused by treponematosis but by leprosy. Today, lepromatous leprosy induced periostitis is rarely seen (Waters, 1990, Resnick, 1995, Lewis *et al.*, 1995). Therefore, it does not seem very probable that all the individuals from Chichester who had suffered from leprosy would also have *M. leprae* induced periostitis. However, we do not know today in what way the disease was expressed or what the nature of the human immune system was some hundreds of years ago (although there is no evidence that it has changed in character). The changes in the individual from burial 88 from Chichester additionally showed signs of a florid osteomyelitis, combined with osteitis and periostitis. These relatively new changes were probably caused secondarily by infection of an ulceration of the skin of the lower leg, which led to a pyogenic osteomyelitis (cf. Waters, 1990, Resnick, 1995).

The second possibility also sounds plausible. As we know, patients in medieval leprosaria frequently suffered not only from leprosy but also from treponemal disease (Ackerknecht, 1963), although see Crane-Kramer (this volume). The microscopic features found in these samples such as polsters and grenzlinie which are characteristic of treponemal disease, in their well developed stages, support this suggestion. Therefore, it is possible that the individuals described in this paper may have suffered additionally from treponematosis, probably endemic syphilis, which produced milder bony changes than those of venereal syphilis (cf. Schultz and Teschler-Nicola, 1987, Schultz, 1994, Kuhnen *et al.*, 1999). However, polsters and grenzlinie are only very poorly developed in these cases described above. Only in the case of Lihou male in whom, with the exception of the periosteal reaction, no signs of leprosy could be identified, could endemic syphilis be suggested as a diagnosis with a relatively high probability. Theoretically, this case from Lihou might indicate that all the six individuals from Chichester suffered additionally from endemic syphilis. However, this does not seem very likely.

Independent of the two possibilities mentioned above, osteoporosis (individual from Chichester burial 48), the enlargement of the medullary cavity and the rarefaction of the compact bone substance (individual from Lihou and probably also the individual from Chichester burial 48) and, particularly, the presence of tangential lamellae in the compact bone substance (individual from Chichester burial

148 and the male from Lihou) were very probably due to disuse atrophy and lack of use of the legs. In other cases, an advanced age could also be responsible for these changes (e.g. the individual from Chichester burial 48).

5. Conclusions

It can be assumed that in these seven cases, the signs of longstanding, i.e. remodelled, new bone formation, represents a primary periosteal inflammation. This inflammatory process was apparently relatively mild because there is no evidence that the compact bone substance was substantially affected. Additionally, there is also evidence of a florid, secondary periostitis (Chichester burial 88). In this case the compact bone substance, as well as the medullary cavity, was affected.

The microscopic analysis of the tibial samples from Chichester and Lihou shows that there is a special pattern of features which is associated with skeletal leprosy. The classification and interpretation of these morphological features, particularly the new built bone formation, is sometimes controversial. However, in summary, the probability is very high that the periosteal changes on the surfaces of the tibial shafts of the individuals from Chichester were caused by infections secondary to leprosy. The changes in the tibia of the male from Lihou are also suspicious of leprosy. However, it is still a possibility that other processes, such as endemic syphilis or inflammatory processes of the deep veins of the lower legs, resulted in these periosteal changes. Additional to the signs of inflammatory processes, there is also in at least two cases, evidence of limited function or even disuse of the affected leg. This also emphasises that the disease process was chronic.

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Table 1: Skeletons selected for analysis by age and sex

Number	Ch 21	Ch 48	Ch 64	Ch 88	Ch 148	Ch 202	Lihou
Sex	M	M	M	M	M	F>>M	M
Age	young adult (17-25 years)	mature adult (older than 45 years)	adolescent to young adult (16-20 years)	young to middle adult (26-45 years)	young to middle adult (26-45 years)	young to middle adult (30-40 years)	young to middle adult (26-45 years)

Table 2: Features used for the diagnosis of leprosy for the selected individuals from Chichester and Lihou

Number	Ch 21	Ch 48	Ch 64	Ch 88	Ch 148	Ch 202	Lihou
Face	+	+	+	+	+	+	-
Hands	+	-	-	-	+	-	-
Feet	+	+	+	+	+	-	-
Lower legs	+	+	+	+	+	+	+

+ = changes present

- = changes absent

Table 3: Bone changes and microscopic features of inflammatory processes in the six individuals from Chichester and the male from Lihou

Features	Chi 21	Chi 48	Chi 64	Chi 88	Chi 148	Chi 202	Lihou
Periosteum	+	+	+	+	+	+	+
Compact substance	-	[+]	-	+	-	-	(+)
Medullary cavity	-	[+]	-	+	-	-	[+]
Recidivation	(+)	+	-	-	-	-	+
Remodelling	+	+	+	+	+	+	+
Slowly growth	+	+/-	(+)	+	+	+	+
Osteoporosis	-	[+]	-	+	-	-	-
Polster-like structures	-	-	+	+	+	-	+
Grenzlinie-like structure	+	-	-	(+)	+	(+)	(+)
Tangential lamellae	-	-	-	-	+	-	+

+ = affected by an inflammatory process/feature present

(+) = not very pronounced, probably affected by an inflammatory process/very slight features probably developed

[+] = changes present, but probably not caused by an inflammatory process

- = not affected by an inflammatory process/feature not present

+/- = uncertain

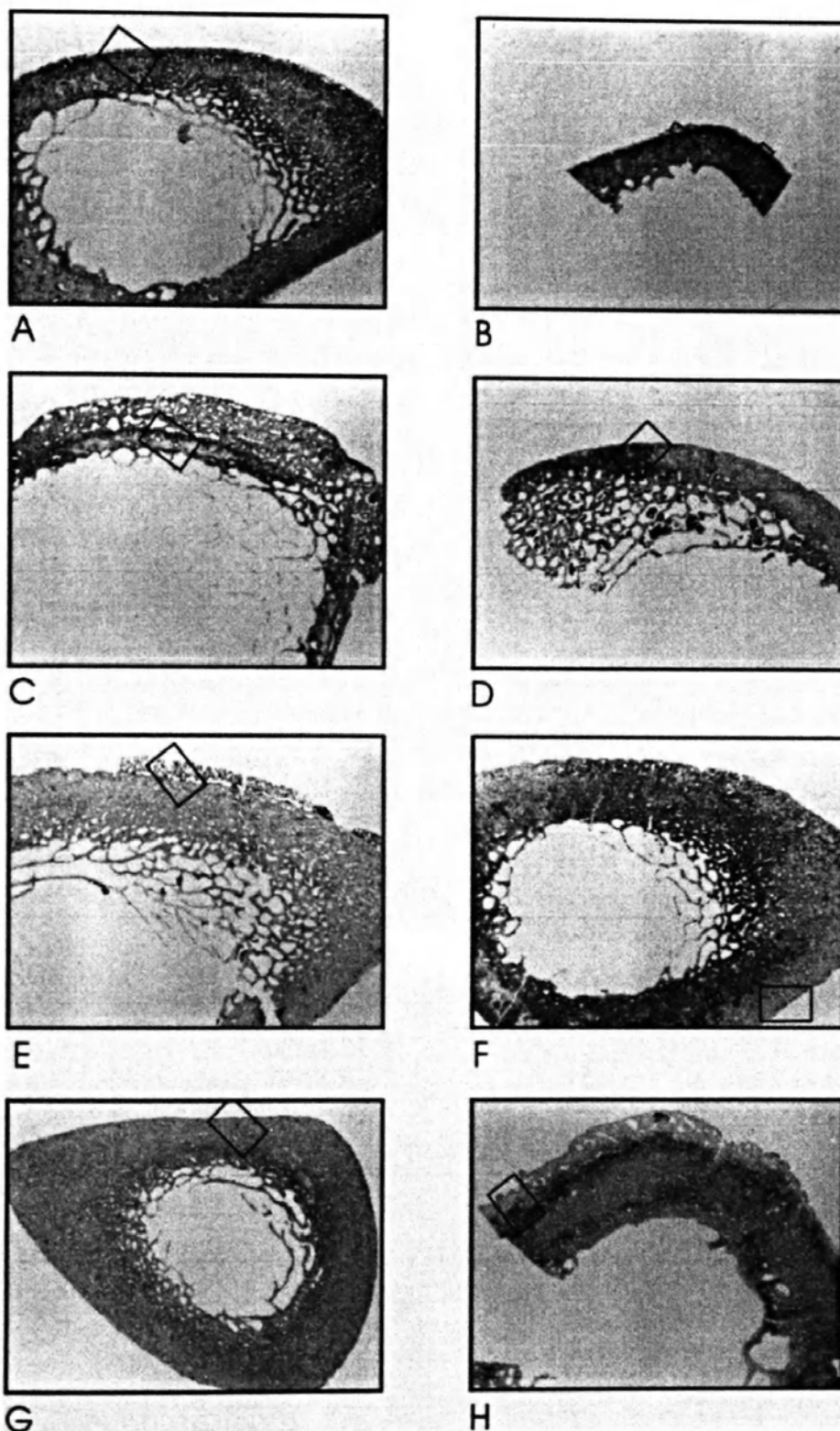


Plate 1:

Thin ground sections (70µm) of samples taken from tibial shafts. All photos are presented at the same scale (approx. 2x)

- A) Chichester 21: Cross section through left tibia (proximal part of sample). The black frame on the medial face marks Figure 7.
- B) Chichester 21: Cross section through left tibia (proximal part of sample). The two black frames mark Figure 6 (right frame) and Figure 8 (left frame).
- C) Chichester 48: Cross section through left tibia. The black frame on the antero-lateral face marks Figure 9.
- D) Chichester 64: Cross section through right tibia. The black frame marks Figure 11.
- E) Chichester 88: Cross section through right tibia. The black frame on the medial face marks Figure 12.
- F) Chichester 148: Cross section through right tibia. The large black frame on the antero-lateral face marks Figure 14; the small black frame in the compact bone substance marks Figure 15.
- G) Chichester 202: Cross section through right tibia. The black frame on the lateral face marks Figure 16.
- H) Lihou male: Cross section through left tibia. The black frame on the medial face marks Figure 19. From the gap in the compact bone substance (left) the sample for scanning-electron microscopy was taken (Fig. 18).

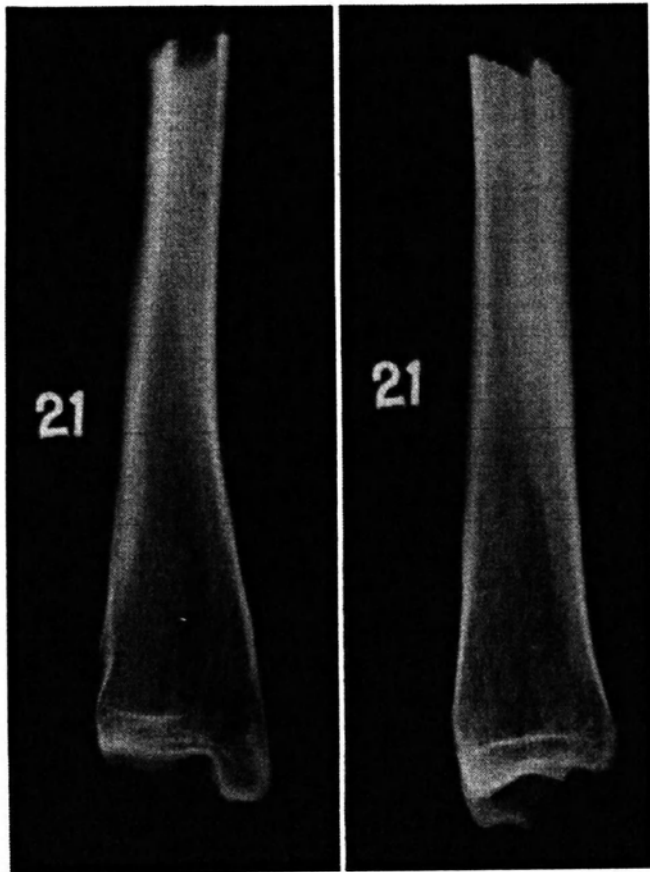


Figure 1: Chichester 21: Radiographic images of periostitis on tibia

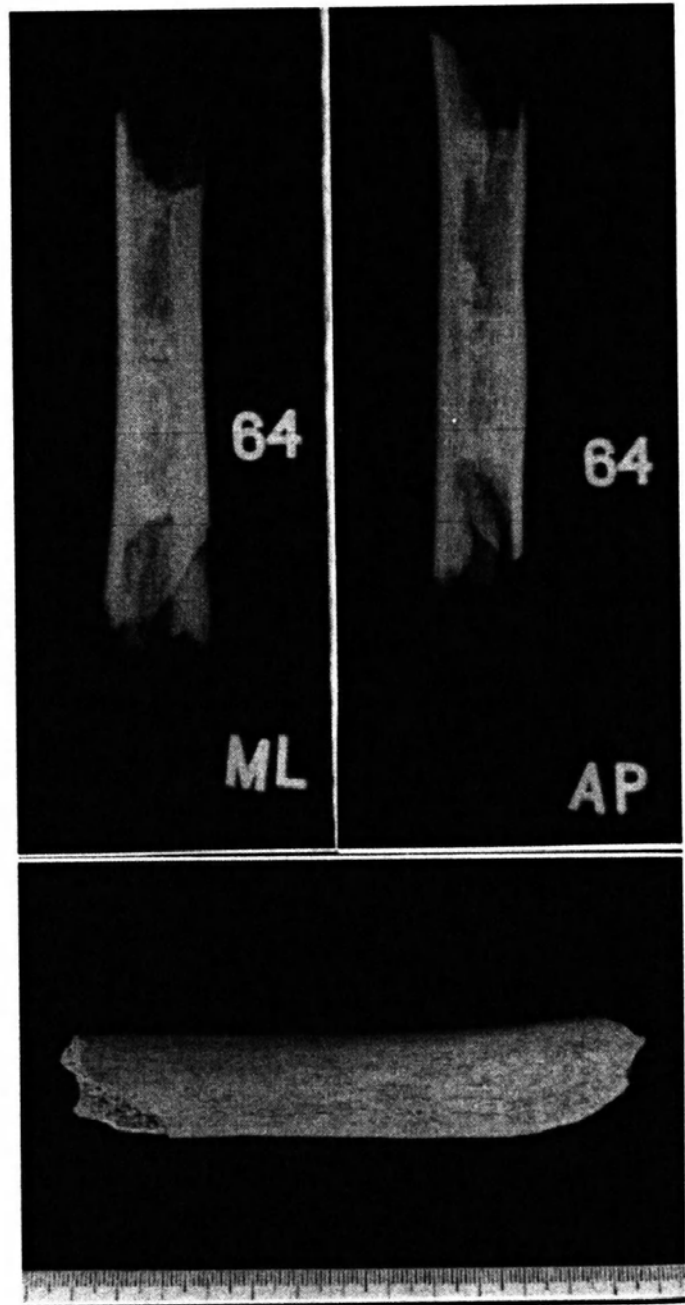


Figure 2: Chichester 64: Macroscopic and radiographic images of periostitis on a fragment of shaft of tibia

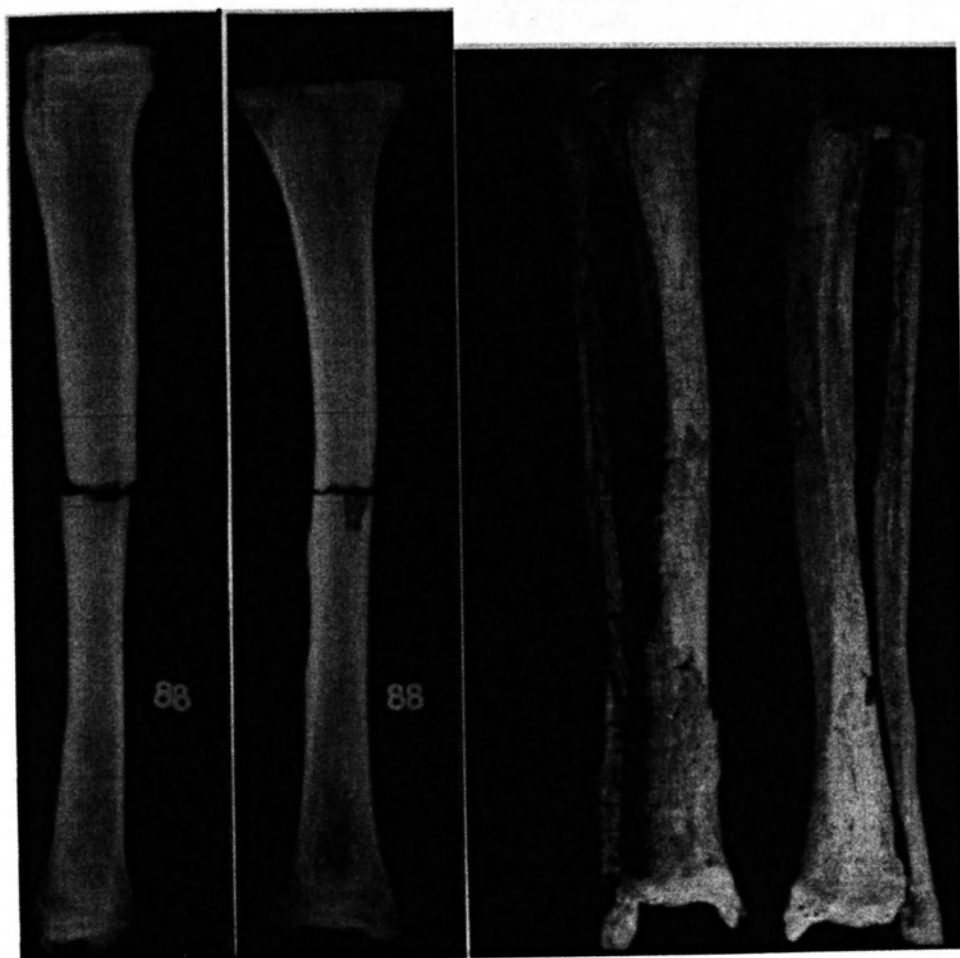


Figure 3: Chichester 88: Macroscopic image of both tibiae and fibulae showing extensive periostitis, and radiographic images of the tibia analysed

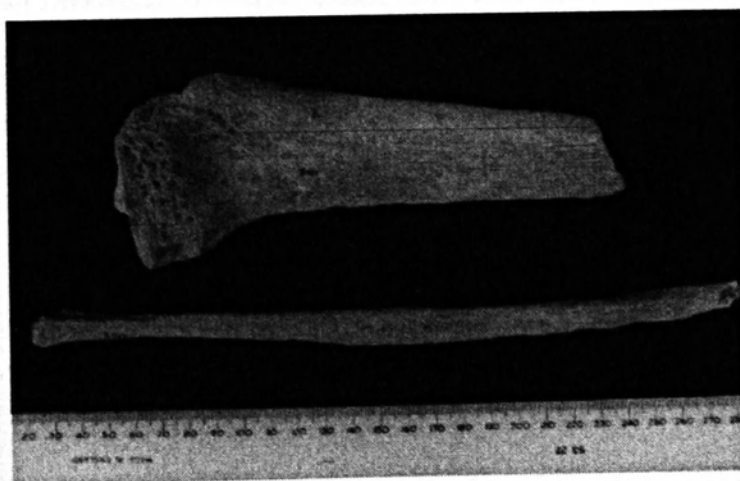
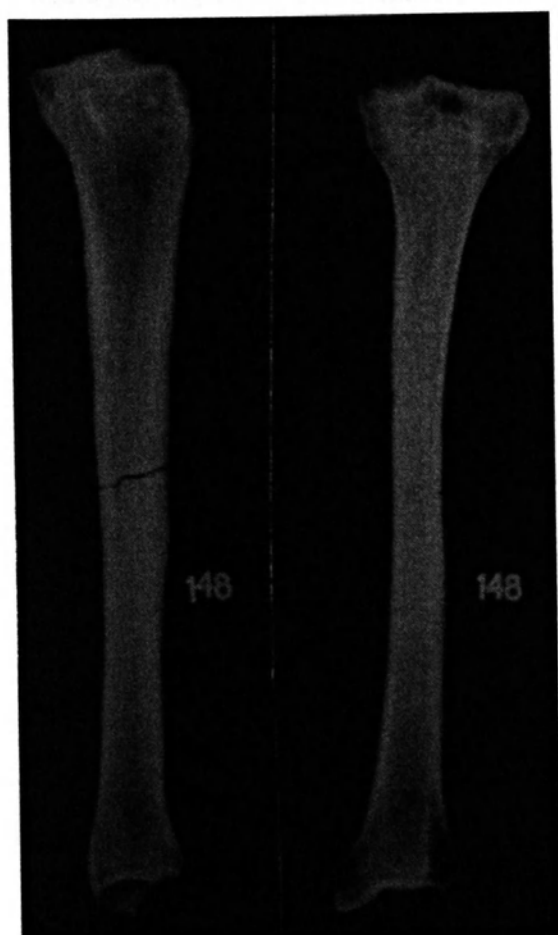


Figure 4: Chichester 148: Macroscopic image of tibia and fibula with periostitis used for analysis, and radiographic image of tibia





Figure 5: Chichester 202: Macroscopic image of tibia with periostitis used for analysis, and radiographic image of same bone

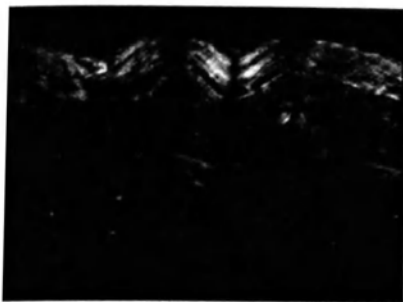


Figure 6: Chichester 21 (distal part of sample). Thin ground section (70µm) viewed by microscope in polarised light. Periosteal bone surface. Well organised secondary layer showing blood vessel impressions. Magnification 100x.

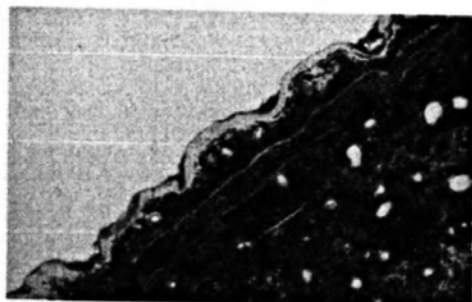


Figure 7: Chichester 21 (proximal part of sample). Thin ground section (70µm) viewed by microscope in plane light. Periosteal bone surface. Well organised secondary layer showing blood vessel impressions and fine border line resembling a grenzlinie. Magnification 25x.

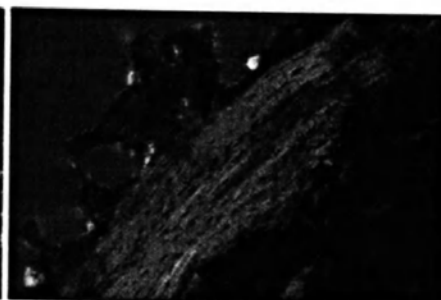


Figure 8: Chichester 21 (distal part of sample). Thin ground section (70µm) viewed by microscope in polarised light using a half-subject red 1st order (quartz) as compensator. Periosteal bone surface. Relatively fresh newly built bone formation (woven bone) on the original external bone surface. Magnification 100x.

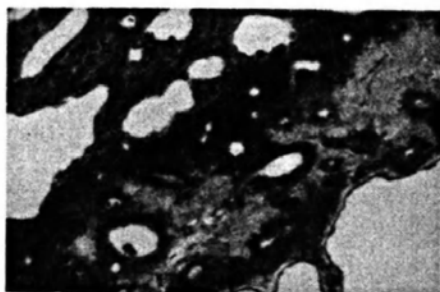


Figure 9: Chichester 48. Thin ground section (70µm) viewed by microscope in plane light. Secondary layer, compact bone substance and endosteal bone surface. Extreme reduction of compact bone substance demonstrating osteoporosis. Magnification 25x.

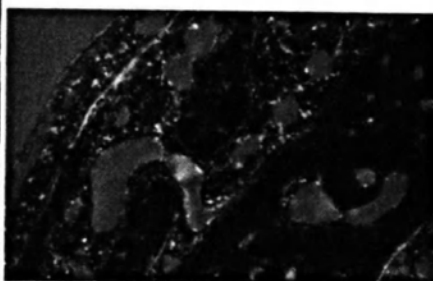


Figure 10: Chichester 48. Thin ground section (70µm) viewed by microscope in polarised light using a half-subject red 1st order (quartz) as compensator. Compact bone substance and periosteal bone surface representing two strata of newly built bone formation. Secondary osteoporosis. Magnification 25x.

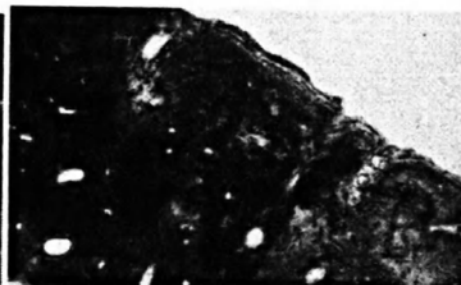


Figure 11: Chichester 64. Thin ground section (70µm) viewed by microscope in plane light. Periosteal bone surface. Very well organised periosteal bone surface showing polster-like structures. Magnification 25x.

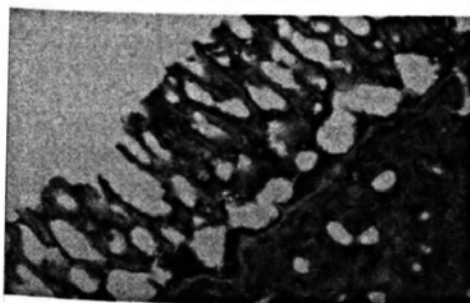


Figure 12: Chichester 88. Thin ground section (70µm) viewed by microscope in plane light. Periosteal bone surface. Product of periostitis (woven bone) on bone surface. Magnification 25x.

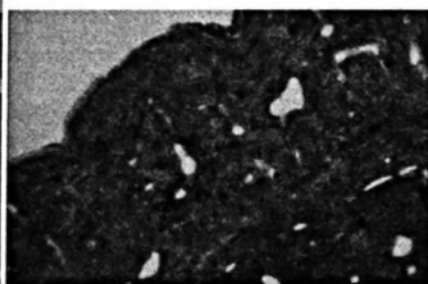


Figure 13: Chichester 88. Thin ground section (70µm) viewed by microscope in plane light. Periosteal bone surface. Very well organised periosteal bone surface showing polster-like structures. Magnification 25x.

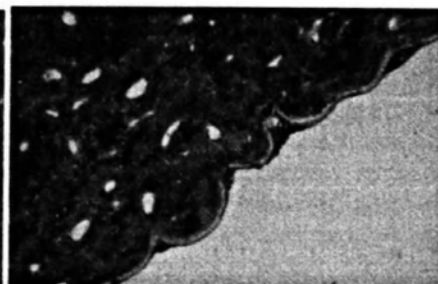


Figure 14: Chichester 148. Thin ground section (70µm) viewed by microscope in plane light. Periosteal bone surface. Well organised secondary layer showing blood vessel impressions and early polster-like structures. Magnification 25x.

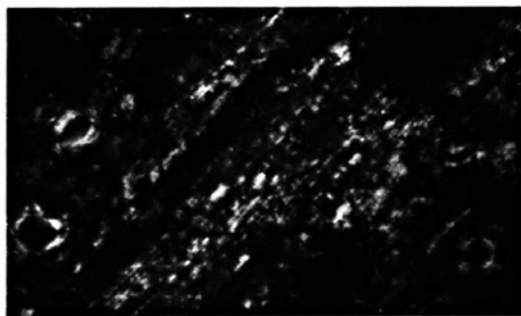


Figure 15: Chichester 148. Thin ground section (70µm) viewed by microscope in polarised light. Compact bone substance. Tangential lamellae suggesting inactivity atrophy. Magnification 100x.

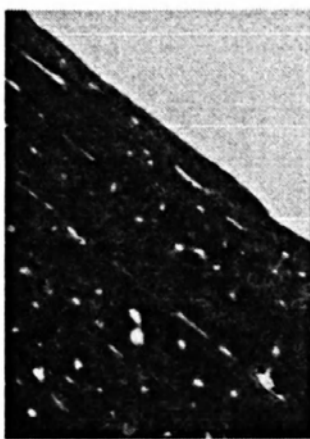


Figure 16: Chichester 202. Thin ground section (70µm) viewed by microscope in plane light. Periosteal bone surface. Between a relatively thick, very well organised secondary layer and the compact bone substance, there is a border line built up by very small, tangentially orientated blood vessel canals. Magnification 25x.

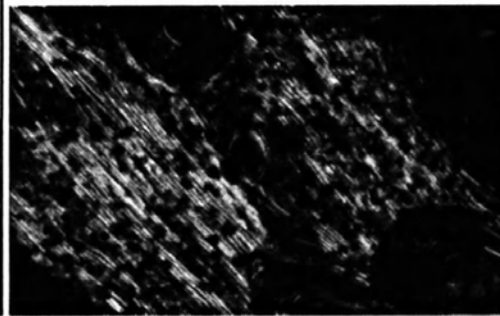


Figure 17: Lihou male. Thin ground section (50µm) viewed by microscope in polarised light. Compact bone substance. Tangential lamellae suggest disuse atrophy. Magnification 100x.

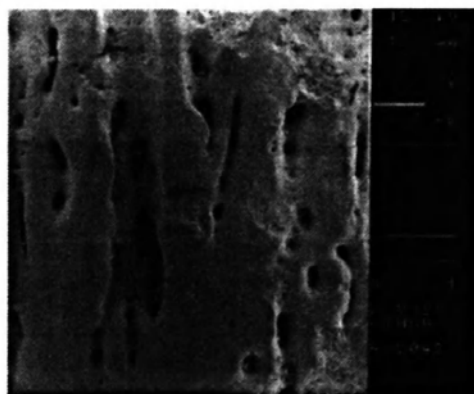


Figure 18: Lihou male. Scanning-electron microscopic image. External surface of the new bone formation. Magnification 12x.



Figure 19: Lihou male. Thin ground section (70µm) viewed by microscope in plane light. Periosteal bone surface. Organised polster-like structures as well as remains of a border line resembling a grenzlinie. Magnification 25x.

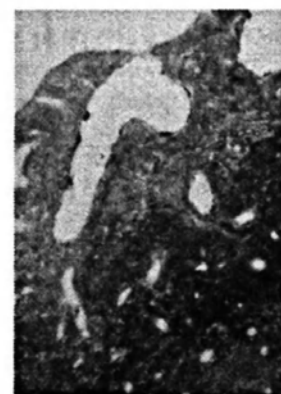


Figure 20: Lihou male. Thin ground section (50µm) viewed by microscope in plane light. Periosteal bone surface. The relatively fresh new bone formation (woven bone) is the product of a periosteal inflammation. Magnification 25x.

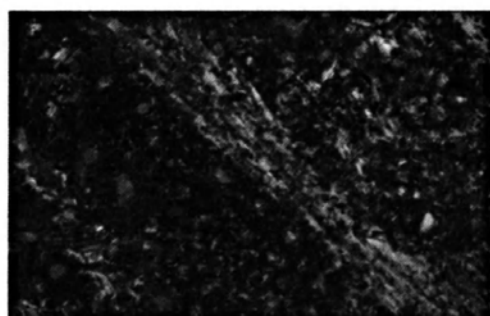


Figure 21: Lihou male. Thin ground section (50µm) viewed by microscope in polarised light using a hilfsobject red 1st order (quartz) as compensator. Cord-like structures in the interior area of the compact bone substance. Magnification 25x.